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Stereoisomeric Styryl Derivatives of Some 4-Quinazolone Alkyl Iodides and Their Bearing upon the Problem of Photosensitizing Dyes

DISSERTATION

SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN THE FACULTY OF PURE SCIENCE OF COLUMBIA UNIVERSITY

By

HELEN CLARK, B.S., M.A.

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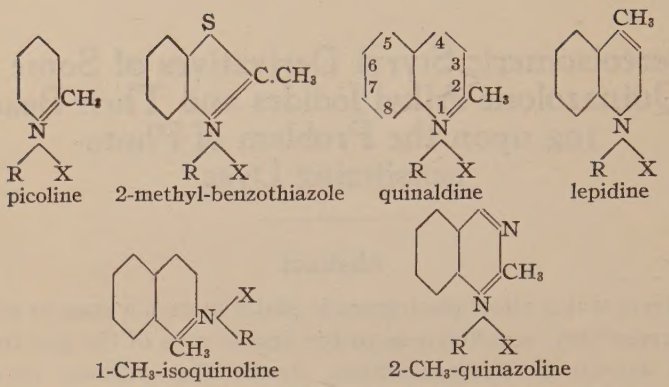
Stereoisomeric Styryl Derivatives of Some 4-Quinazolone Alkyl Iodides and Their Bearing upon the Problem of Photosensitizing Dyes

Abstract

Dyes which affect photographic plates in such a manner as to increase their sensitiveness to the visible rays of the spectrum are known as photosensitizing dyes. The ordinary photographic plate, which is extremely sensitive to ultra-violet, violet and blue rays, does not give a correct rendering of colored objects. In order that photographs should correctly translate into monochrome the luminosity value of colors as seen by the eye, it is necessary to use a plate treated with a photosensitizing dye. These special photographic plates bring out the details of the object to be photographed in their true relationship to each other. This is shown very well in photographs of furniture, microscopic sections, and landscapes taken through great aerial distances, as in aerial reconnaissances. Another important use is that photographs may be made with infra-red rays, as would be necessary in astronomical work.

While some azo colors, roseaniline dyes and phthaleins have been used for this purpose, all except erythrosin have been superseded by the "cyanine" dyes. These dyes are derived from cyclo-ammonium bases having a methyl group in the 2 or 4 position either condensed with themselves or other suitable substances. The bases most commonly used are those of the quinoline series, but pyridine and benzothiazole derivatives have also been found useful. In general, a nitrogen heterocyclic compound which has a methyl group in the 2 position when condensed in an alkaline solution yields a photosensitizing dye. Because of the structural relationship between quinaldinium and quinazolinium bases, it seemed desirable to study the latter in order to throw additional light upon the connection between chemical structure and photosensitizing properties and if possible to prepare new photosensitizing dyes.

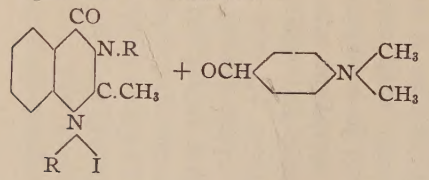


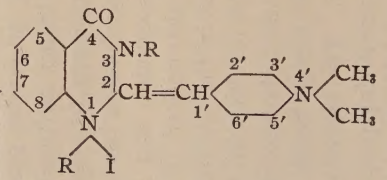
Alkyl Halides of Various N-Heterocycles

The quinazolines selected for this study were 2,4-dimethyl-quinazoline, 2-benzylidene-4-methyl-quinazoline, 2-phenyl-4-methyl-quinazoline, because of their relationship to quinaldine, lepidine and isoquinoline derivatives. On attempting to prepare the alkyl halide derivatives of these quinazolines no crystalline addition compound could be isolated under the experimental conditions used. 2,4-Dimethyl-quinazoline did not condense with benzaldehyde or with *p*-dimethylaminobenzaldehyde in the presence of a catalyst. There does not seem to be any adequate explanation for the non-reactivity of the methyl groups in this heterocycle.

It was necessary, therefore, to use some alkyl halide addition compounds of various 4-quinazolones previously prepared by Bogert and Geiger. The methyl iodides of 2-methyl-4-quinazolone, 3-methyl-4-quinazolone, 2,3-dimethyl-4-quinazolone, 2-methyl-3-ethyl-4-quinazolone and also the ethyl iodide derivative of 2,3-dimethyl-4-quinazolone were chosen in order if possible to determine the structure of the condensation products formed, and the effect of various alkyl groups in the 1 and 3 positions on photosensitizing properties. When the 4-quinazolonium bases were condensed with *p*-dimethylaminobenzaldehyde in the presence of piperidine, bright red crystalline dyes were isolated in each case except with 3-methyl-4-quinazolone methyl iodide which did not condense with *p*-dimethylaminobenzaldehyde. In an attempt to obtain better yields, acetic anhydride was tried as a condensing agent. The crystal-

Piperidine Condensation

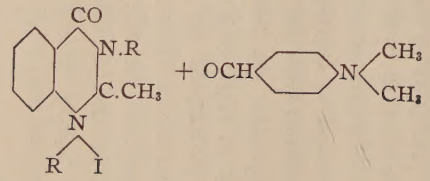


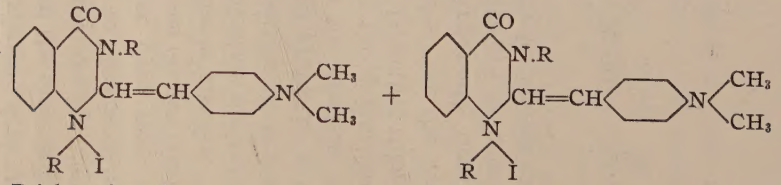


Bright red needles

Identical

Acetic Anhydride Condensation





Bright red needles
0.25 hour at 145–150°
Lower melting isomer

Reddish-purple needles
2 hours at 120°
Higher melting isomer

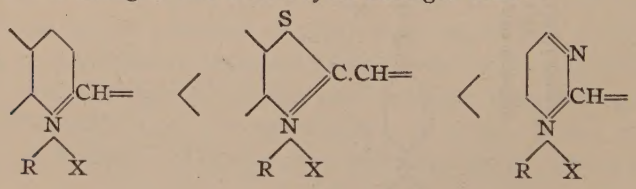
Heat for 2 hours at 120°

line mass which separated proved to be a mixture of geometrical isomers. The lower melting forms, bright red needles, are identical with those isolated from the piperidine condensations. The higher melting isomers, red purple needles are undoubtedly the stable form, since the lower melting ones can be transformed into the higher melting form by prolonged heating at 120° in acetic anhydride. It was not possible to change the stable form into the labile form under the experimental conditions employed. By changing the time and temperature of heating in acetic anhydride, it was possible to prepare one isomer to the exclusion of the other. These substances are weak substantive dyes, dyeing silk a pale orange which changes to yellow in soap solution, fugitive to sunlight.

Preparation of bromine derivatives of each high and low melting substance showed them to be isomers. On treating a cold chloroform solution of the lower melting dye with bromine, an orange product, the tribromo derivative was isolated. The higher melting form yielded the same tribromo derivative.

Attempts to employ condensation reactions with these 4-quinazolonium bases analogous to those used in the preparation of isocyanine and carbocyanine dyes were unsuccessful. It was also noticed that these bases do not condense with themselves in the presence of pyridine or alkalies.

The results with the quinazolonium derivatives studied indicate that photosensitizing properties are dependent upon some other factor beside a 2-methyl group in a cyclo-ammonium base. The carbonyl group in the position 4 does not affect the sensitizing properties, since the quinazolines do not exhibit these properties either. 1,1′-Dimethyl-thioisocyanine iodide has weaker sensitizing properties than the corresponding 1,1′-dimethyl-isocyanine iodide. Apparently then the nature of the heterocyclic nucleus exerts a marked influence, the depressing effect increasing as the heterocycle changes thus:



2-*p*-Dimethylaminostyryl-pyridine methyl iodide is one of the most powerful sensitizers for green yet noted, but tests on several of the dyes derived from the 4-quinazolonium bases show negative sensitizing properties. This is probably due not only to the nature of the heterocyclic system, but also to the depressing effect of substitution in the 3 and 4 positions as previously noted by Pope and Mills in their work on the "cyanines."

The following new substances were prepared in the course of the work:

Stable and labile forms of the methyl iodides of

2-*p*-dimethylaminostyryl-4-quinazolone

2-*p*-dimethylaminostyryl-3-methyl-4-quinazolone

2-*p*-dimethylaminostyryl-3-ethyl-4-quinazolone

and also

2-*p*-dimethylaminostyryl-3-methyl-4-quinazolone ethyl iodide

tribromo - 2 - *p* - dimethylaminostyryl - 3 - methyl - 4 - quinazolone methyl iodide

tribromo - 2 - *p* - dimethylaminostyryl - 3 - ethyl - 4 - quinazolone ethyl iodide.

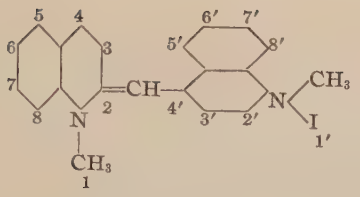
Introductory and Historical

The effect which certain dyes have on photographic plates, thereby increasing their sensitiveness to the less refrangible rays of the spectrum, has increased the interest in their preparation and the study of their structure. The most important dyes in this connection are the "cyanine" dyes prepared from quinolinium salts and their derivatives. Some of these dyes[1,2] were introduced into the trade by Müller at Bôle and Ménier at Paris, but owing to their fugitiveness to light they never became popular. Vogel[3,5] noticed that Wortley collodiobromide dry plates, which were stained with a yellow dye to prevent halation, showed a maximum photographic sensitiveness in green, and when the plate was washed, the green sensitiveness was destroyed. On trying coralline, magenta, naphthalene red, methyl violet, and cyanine, he found that these also had similar effects. Later these results were confirmed by Becquerel[4] who discovered the sensitizing action of chlorophyll. Since then many new "cyanine" dyes have been prepared[3,5]

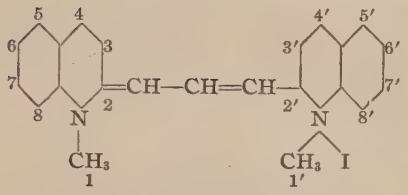
and literally hundreds have been examined[15] for photosensitizing properties, but only a few have proved of any considerable worth. Recently it has been discovered[25,31,34,36,37,39] that other cyclo-ammonium compounds when coupled with themselves or other suitable substances may also be used as sensitizers. Therefore it seemed desirable to determine whether derivatives of quinazolinium compounds would prove of value as photosensitizing dyes.

Ordinary photographic plates coated with gelatin emulsion containing silver bromide are affected only by blue, violet, and ultra-violet light. If small amounts of certain dyes are added to the emulsion on the photographic plate, or if the plate is bathed in the dye solution, the photographic plate may become sensitive to green-yellow (orthochromatic plates), and also to orange-red (panchromatic plates). In order that a dye may be eligible for this class, it is necessary (1) that it combine with the silver bromide itself; (2) that it be a substantive dye; (3) that it be soluble in water, or at least capable of forming a fairly stable colloidal solution with it; (4) that the gelatin should not be stained by it. In general, the center of the region which is sensitized by the dye lies twenty millimicrons farther toward the red than the center of the absorption band of the dye,[15] namely, dyes which sensitize for yellowish-green are reddish in color (erythrosin); dyes which sensitize for orange are purple (cyanine); and red sensitizers are green (pinacyanol).

The isocyanine and carbocyanine dyes have proved to be of more value than cyanine itself. A review of the work of Pope and Mills and their co-workers discloses some interesting facts. An examination of the spectographs shows that total sensitiveness diminishes steadily as the moelcular weight of the dye increases. This is contrary to Nietzki's rule[9] which states that an increase in molecular weight shifts absorption toward the red. Changing the alkyl halide radical from methyl to propyl diminishes the sensitiveness of the dye, and there is a distinct displacement of the maximum toward the less refrangible region of the spectrum.



Isocyanine



Carbocyanine

The sensitizing effect of 1,1′-diethylisocyanine iodide is enhanced by introduction of a methyl group in the 6 position but depressed when the same group is introduced in the 2 position. Introducing an amino group in 5, 6, or 6′ position in 1,1′-dimethylisocyanine iodide shows markedly augmented sensitizing power. On the other hand, the introduction of an acetyl, cinnamoyl, cyano, or phenyl group depresses the sensitizing effect, and in the case of the two latter inhibits sensitization. Substitution in the 2′, 3′, or 4′ position gives feeble sensitizers. These results are significant when considered in connection with the suggested molecular weight of the isocyanines. The interaction of a compound of this formula with light waves would be, in accordance with modern chemical views, related to the presence in the molecule of two basic groups, one saturated, the other unsaturated connected by a chain of conjugated ethylenic linkages. It is reasonable to suppose that loading ethylenic linkages with methyl, cyanogen, or phenyl groups, inhibits the interaction. The same argument applies to substitution in the 3′, and 4′ positions. It may also be predicted that all the 2′, 3′, 4′ substituted isocyanines will prove to be feeble sensitizers. Despite these conclusions, it is still necessary, however, to test each dye carefully as to its real value as a sensitizer.

Hofmann[7] noticed that bases of the benzothiazole series could be substituted for quinolinium and quinaldinium bases. He was able to prepare dyes analogous to the "cyanine" type by using alkyl halide benzothiazoles and alkali. Later König[25,34] found that he could obtain color materials similar to the "cyanines" by condensing quinaldinium or lepidinium salts with *p*-dimethylaminobenzaldehyde in the presence of piperidine. These substances were not closely investigated, as this condensation was carried out with the idea of proving the structure of the isocyanines. Barbier,[31] also, prepared a number of these dyes, but failed to mention their photosensitizing properties.

In their extended investigations on photographic sensitizers, Pope and Mills,[36] observed that unlike other classes of dyestuffs the most useful ones were those of simple structure, and that one of the original materials was usually a cyclo-ammonium compound. It seemed advisable to them, therefore, to test this theory further by using one of the simpler cyclo-ammonium bases, namely, picoline methyl iodide. This substance was condensed with *p*-dimethylaminobenzaldehyde, using piperidine as a condensing agent. They obtained 2-*p*-dimethylaminostyryl-pyridine methiodide, a compound forming bright red prisms with a blue reflex. Its aqueous solution dyes silk a bright orange-yellow fugitive to light. It proved to be one of the most powerful sensitizers for green yet noted.

In substituting the quinazoline heterocycle for that of the quinoline, the members of this group which most naturally suggested themselves were quinazoline; 2-methyl-quinazoline; 4-methyl-quinazoline; 2,4-dimethyl-quinazoline. The 2-methyl and 4-methyl[46] quinazolines are somewhat difficult to prepare. The experiments were therefore carried out with 2,4-dimethyl-quinazoline.[11] There are only a few alkyl halides of quinazoline bases recorded in the literature, and these are only formed in small amounts and with considerable difficulty. Bischler and Barad[10] found it possible to prepare an alkyl halide of 2-methyl-4-phenyl-quinazoline. Gabriel[29] reported that he was able to obtain a methyl iodide derivative of quinazoline, as a yellowish crystalline material, which when heated started to decompose

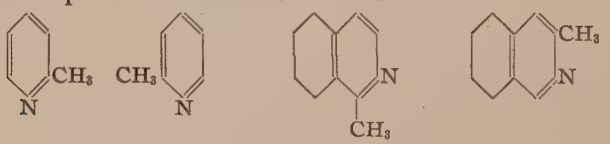
at 115°, melting at 125–127°. He reports that it was difficult to handle and decomposed easily.

All attempts to prepare a crystalline quaternary alkyl halide of 2,4-dimethyl-quinazoline proved to be unsuccessful. Methyl iodide was heated with 2,4-dimethyl-quinazoline in a sealed tube for several hours at 110°. A dark green amorphous material was obtained. On prolonging the heating for five hours at a higher temperature, a light brown hard amorphous mass was formed. Although many solvents and mixtures of solvents were tried, it seemed impossible to crystallize either of these substances. In some cases dimethyl sulfate[40,44] has shown itself to be a better agent than alkyl halides for the preparation of quaternary salts, therefore it was tried, but although the conditions of experimentation were changed as to length of time of heating, temperature and use of solvent, it also was ineffectual in giving a crystalline quaternary salt. It was thought that possibly the failure to prepare a quinazolinium derivative might be due to the basicity of 2,4-dimethyl-quinazoline. It was decided, therefore, to introduce a more negative group on the heterocyclic nucleus. A quaternary derivative of 2-methyl-4-phenyl-quinazoline having been prepared previously,[10] a similar attempt was made to prepare the quaternary salt of 4-methyl-2-phenyl-quinazoline. After heating this compound with methyl iodide in a sealed tube for some time, the original quinazoline remained unchanged. The tube was resealed and heated for a considerably longer period, but on opening it the quinazoline still remained intact. One more attempt was made to prepare a cycloammonium derivative of 2-styryl-4-methyl-quinazoline. This was an orange amorphous substance, but owing to its tendency to form a sticky mass, it was impossible to crystallize it.

In order to determine if the methyl groups in 2,4-dimethyl-quinazoline were reactive, it was heated with benzaldehyde at 110° for three hours in the presence of zinc chloride, but no condensation occurred. On raising the temperature to 200°, a tarry substance was obtained which was slightly soluble in dilute acids but no crystalline material could be isolated. When 2,4-dimethyl-quinazoline was treated with 2-*p*-dimethylamino-

benzaldehyde in presence of small quantity of piperidine no condensation occurred even after heating for ten hours. Both of the original constituents could be recovered unchanged.

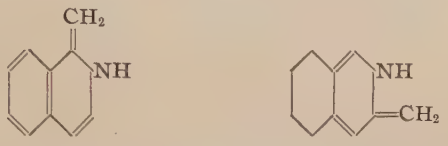
The results obtained with these quinazoline derivatives are quite interesting in view of some data published recently by Mills and Smith.[41] They suggest that the reactivity of the 2-methyl group in the bases of pyridine and quinoline series may be due to its being associated, as represented in Körner-Dewar formula for pyridine, with a $-\overset{|}{C}=N-$ group. If it is true that the effect of the $-\overset{|}{C}=N-$ on the methyl group in the $CH_3-\overset{|}{C}=N-$ corresponds with that of the carbonyl group in the grouping $CH_3-\overset{|}{C}=O$ of the methyl ketones, then it is possible for two distinct chemical forms of α-picoline to exist, one (1) form having a reactive, while the other (2) would have a non-reactive methyl group. In order to test this theory 1-(3) and 3-methylisoquinoline (4) were used because of the improbability of obtaining the two forms of α-picoline separate from each other. When benzaldehyde was condensed with these substances in the presence of zinc chloride, it was possible to obtain a styryl derivative with 1-methylisoquinoline but not with 3-methyl isoquinoline. Similar results were obtained when other pairs of isomerides were used.



(1) (2) (3) (4)

"It is possible, therefore, to consider the difference in reactivity shown by a methyl group in these heterocyclic bases according as it lies on one side or the other of the nitrogen atom not only from the point of view of the nitrogen-carbon linkages, but also from the different but closely related aspect of tautomeric change. The contrast in properties observed in the pairs of isomerides studied may be regarded as indicating that passage into a reactive form is possible when the methyl group

is in the one position, but not when it is in the other." The conclusion may be drawn that only such change takes place in the heterocyclic nucleus as is compatible with retention of the full aromatic character of the benzonoid nucleus.

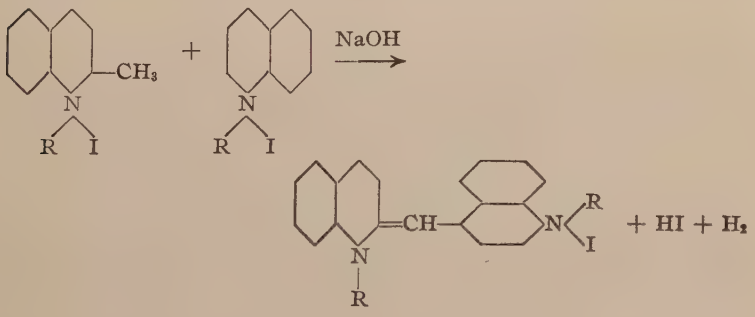


In the case of the 2,4-dimethyl-quinazoline, the methyl groups are in the position of greatest reactivity and the heterocyclic ring may undergo tautomeric change without disturbing the benzonoid nucleus, still it is not possible to condense it with

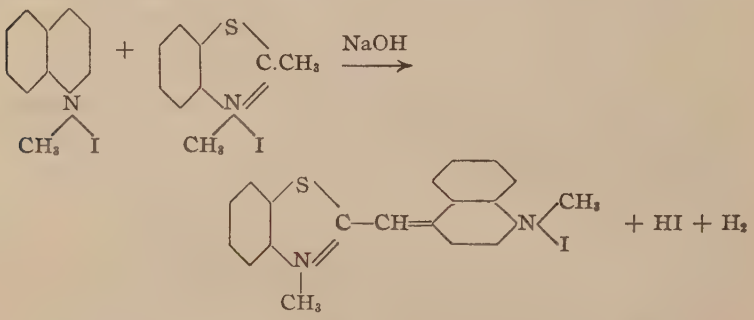
benzaldehyde in the presence of zinc chloride, nor with *p*-dimethylaminobenzaldehyde in the presence of piperidine. There does not seem to be any adequate explanation for the non-reactivity of the methyl groups in this heterocycle.

Since the cyclo-ammonium derivatives of the quinazolines studied could not be prepared under the experimental conditions employed the quaternary salts of some of the 4-quinazolones were used because they could be prepared in quantity.[26]

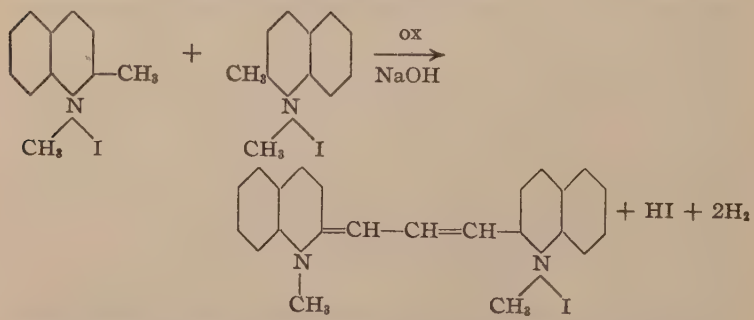
When quinoline and quinaldine alkyl halides are condensed together in the presence of alkali, an isocyanine dye results.[32]



In substituting a benzothiazole compound for one of the quinolinium derivatives in the isocyanine dye; it was discovered that only the quinaldinium nucleus could be replaced.[39] 1-Methylbenzothiazole methyl iodide heated in the presence of sodium hydroxide condenses to form 1,1′-dimethyl-thioisocyanine iodide. On the other hand when benzothiazole methyl iodide



was condensed with quinaldine methyl iodide no thioisocyanine was formed. This may possibly be due to the instability of the pseudo-bases derived from benzothiazole alkyl iodides. The same condition was found to hold for the quinazolonium salts. On condensing quinaldine methyl iodides with 2,3-dimethyl-4-quinazolone methyl iodide, instead of obtaining a dye of the isocyanine type, a small amount of 1,1′-dimethyl-carbocyanine iodide was isolated. When the converse was



tried, namely, the substitution of 2,3-dimethyl-4-quinazolone methyl iodide for the quinaldinium salt, a small amount of a brown substance with a greenish reflection was isolated. A

microscopic examination showed this to contain a mixture of at least three different compounds. Owing to the small yields, which were never more than 0.3 gram from ten grams of original material, and the expense of the iodides used, the attempt to prepare dyes analogous to the isocyanine was discontinued.

In their study of the benzothiazole series, Mills and Braunholtz observed that they could condense two benzothiazole bases together in the presence of pyridine.[39] The dye which they isolated, because of its similarity to the isocyanines, they named thiocyanine. All attempts, however, to condense the quinazolinium salts with each other resulted in failure. The experimental conditions were changed in a variety of ways, and several different condensing agents employed, such as pyridine, sodium hydroxide, sodium ethylate, sodium sulfide with chloroform or formaldehyde, but in each experiment the quinazolinium derivatives were recovered in quantitative amounts.

Neither of these lines of investigation offered much encouragement, and since a few of the condensation products of *p*-dimethylaminobenzaldehyde and the quaternary alkyl halides exhibited marked sensitizing properties it seemed advisable to study this condensation reaction in connection with the quinazolonium bases. The 4-quinazolones studied were selected because their reactions would aid in determining the structure of the derivatives, and also show the effects of various groups on the photosensitizing property of the dyes. Preliminary experiments on the dyeing and sensitizing properties of the dyes prepared showed that the grouping —C(=O)—N—C=N— of the 4-quinazolones has a more marked depressing effect, than the grouping —S—C=N— of the benzothiazoles.[37,39] The dyes derived from benzothiazoles, on the other hand, are not as powerful sensitizers as those of the quinoline series. The dyes obtained from the 4-quinazolones which were tested show practically no photosensitizing powers, and are weak substantive dyes. That the depressing effect of the quinazolone nucleus is not unusual, is shown in the study of 4-quinazolone-2-phthal-

one,[27] a dye analogous to "quinoline yellow" but exhibiting only feeble dyeing properties in contrast to its analogue. Another factor in the depressing effect is the increase in molecular weight of the quinazolonium derivative. 2-*p*-Dimethylaminostyryl-pyridine methyl iodide[36] is a strong green sensitizer, while 2-*p*-dimethylaminostyryl-quinoline methyl iodide[25,34,31] and other analogous compounds apparently have no such marked sensitizing power, although these have not been investigated fully.

The first condensation reactions with *p*-dimethylaminobenzaldehyde were carried out in alcoholic solution using piperidine as a condensing agent. Beautiful bright red needle-like crystalline dyes were obtained from 2-methyl-4-quinazolone methyl iodide; 2,3-dimethyl-4-quinazolone methyl iodide; 2,3-dimethyl-4-quinazolone ethyl iodide; 2-methyl-3-ethyl-4-quinazolone methyl iodide; but no condensation occurred with 3-methyl-4-quinazolone methyl iodide. The yields of dye were small except in the case of the derivative of 2,3-dimethyl-4-quinazolone methyl iodide, probably because of the greater solubility of the other quinazolonium bases and their derivatives.

König and Treichel[34] observed that in condensing *p*-dimethylaminocinnamic aldehyde and quinaldine perchlorate that acetic anhydride was a better condensing agent than piperidine. Another experiment was tried in which one mole of *p*-dimethylaminobenzaldehyde and one mole of 2-methyl-4-quinazolone methyl iodide were heated for a time in acetic anhydride. Instead of a bright red substance separating out, a reddish-purple crystalline one was isolated. This substance melted about 50° higher, was less soluble, and proved to be more difficult to purify than the bright red compound. After considerable difficulty (principally that of separating the mixture) it was purified, and analysis gave the same empirical formula as the lower melting substance. On repeating the experiment, it was noticed that if the temperature was raised, and the time of heating shortened, a mixture of substances was obtained. When the mixture was separated, a bright red compound and a reddish-purple one were found. The red com-

TABLE I

PHYSICAL PROPERTIES OF DYES FROM ACETIC ANHYDRIDE CONDENSATION REACTIONS

4-Quinazole alkyl halide		Product		M. p. (corr.)	Color
2-CH_3-4-quinazolone	CH_3I	2-*p*-diCH_3aminostryryl-4-quinazolone	CH_3I	214.0°	Bright red
				265.7°	Reddish-purple
3-CH_3-4-quinazolone	CH_3I	.....		....	.....
2,3-diCH_3-4-quinazolone	CH_3I	2-*p*-diCH_3aminostyryl-3-CH_3-4-quinazolone	CH_3I	216.0°	Bright red
				263.5°	Reddish-purple
2,3-diCH_3-4-quinazolone	C_2H_5I	2-*p*-diCH_3aminostyryl-3-CH_3-4-quinazolone	C_2H_5I	205.5°	Bright red
				264.7°	Reddish-purple
2-CH_3-3-C_2H_5-4-quinazolone	CH_3I	2-*p*-diCH_3aminostyryl-3-C_2H_5-4-quinazolone	CH_3I	212.0°	Bright red
				255.0°	Reddish-purple

pound on mixed melting point, was found to be identical with that isolated in the piperidine condensation. In studying the formation of these compounds, it was noted that heating for two hours at 120° (±2°) caused the formation of the higher melting substance, while the lower melting one could be formed at a temperature of 145–150° and heating for ten to fifteen minutes. The lower melting substance, if heated in acetic anhydride for a time (one and a half to two hours) at 120° (±2°), was completely transformed into the higher melting one. Attempts to change the higher melting substance into the lower melting form were unsuccessful.

On condensing the other 4-quinazolonium bases with *p*-dimethylaminobenzaldehyde in acetic anhydride, similar results were obtained. In each case it was possible to isolate two derivatives, a bright red one (low melting) and a reddish-purple compound (high melting).

In view of the work by König and Treichel,[34] the behavior of the quaternary alkyl halides of 4-quinazolones with acetic anhydride is of interest. They do not record the formation of more than one compound in their condensation reactions with quinaldinium derivatives and *p*-dimethylamino-cinnamic aldehyde in acetic anhydride.

The probable structure of the dyes is given in the introductory abstract. Condensation reactions with *p*-dimethylaminobenzaldehyde show that the reactive alkyl group is in the 2-position. The only 4-quinazolonium alkyl halide which failed to react with *p*-dimethylaminobenzaldehyde was the 3-methyl-4-quinazolone methyl iodide, and from this reaction both of the original constituents could be recovered in quantitative amounts. There is no evidence of the alkyl group wandering, for the derivatives of 2,3-dimethyl-4-quinazolone ethyl iodide, and 2-methyl-3-ethyl-4-quinazolone methyl iodide are not identical (see Table I), although they are place isomers.

That the reddish-purple dye is the stereoisomer of the bright red dye has been confirmed by preparation of the same bromine derivative from each. From the work of Stoermer [21,22,24,28,30] it seems probable that the more deeply colored, and the higher melting reddish-purple dye is the stable form, while the

labile form is the bright red dye. When the lower melting isomer is treated with bromine in a cold chloroform solution, the deep red solution gradually loses its color, and becomes a cloudy orange. On evaporation of the solvent, an orange amorphous powder remains. This, on examination under the microscope, was found to be a mixture of a light orange material, and a red one. When the mixture was separated and analyzed, it was shown to contain a tribromo derivative and some unchanged red dye. The higher melting isomer on similar treatment also yielded a tribromo derivative. These substances on mixed melting point proved to be identical. It is interesting to note that Bogert, Beal, and Amend[23] found that when 2-styryl-4-quinazolone was brominated in chloroform, or glacial acetic acid solution, they obtained a monobromo substitution product instead of a dibromo addition product as they had expected. The dyes described in this paper apparently add bromine more readily. This increased activity may be due to the presence of the alkyl halide. Further work on the alkyl halide derivatives is in progress.

Experimental Work

A. Quinazolines

***o*-Nitroacetophenone.**[16]—The method used for the preparation of this compound was adapted from that recommended by Camp. 2000 grams of fuming nitric acid (sp. gr. 1.50) agitated by a mechanical stirrer were cooled to —8° C., and 200 grams of acetophenone were added gradually enough to keep the temperature below —5° C. After all the acetophenone had been added, the mixture was poured with stirring into two liters of ice and water. This caused the meta-nitroacetophenone to separate out as a light yellow plastic mass, which was removed by filtration. After sucking the meta compound as dry as possible, the yellowish-green mother liquor was neutralized with sodium carbonate. The yellowish-brown oil, chiefly ortho-nitroacetophenone, was extracted with ether. After drying the ethereal solution with calcium chloride, and evaporating the ether, the oil was distilled under diminished pressure. *o*-Nitroacetophenone, a pale yellow oil with slight odor, distilled at the following temperatures and pressures:

164–165° at 19 mm.	147–148° at 7 mm.
154–155° at 12 mm.	142–144° at 3 mm.

Camp records the following boiling-points:

167–168° at 21 mm.
160–161° at 16.5 mm.
154–155° at 12 mm.

Camp reports a yield of *o*-nitroacetophenone of 44.5% but fails to state the purity of his product. The best yields of pure product obtained by us varied from 28% to 29.5%. It was not possible to free the ortho compound entirely from the meta by distillation, since the latter distils at 167° at 18 mm.[16] If after distillation, the ortho product was allowed to remain in the refrigerator for a time, considerable meta crystallized out. The mixture was then filtered and the oil redistilled. In this manner, it was possible to free the ortho compound of practically all of the meta. Since the meta does not form a cyclic substance in the following reactions, it was not necessary to redistil.

o-**Aminoacetophenone.**—The ortho compound prepared above was reduced with tin and 33% hydrochloric acid as recommended by Camp.[18] 30 grams of *o*-nitroacetophenone and 100 grams of conc. HCl (33%) were added drop by drop to 50 grams of granulated tin, keeping the reaction mixture cooled to 40°. The amino compound was freed from the tin salt by distillation with steam and treated in the usual manner. Yields of reduction compound were 50 to 75%. Although various modifications of the method employed were tried, the yield was not improved. The amino compound is a light yellow oil with an extremely sweet persistent odor. It distils under diminished pressure at 112–114° at 5 mm., and 109–111° at 3 mm. The boiling point recorded in the literature is 125° at 15 mm.[18]

o-**Acetaminoacetophenone.**—In a typical experiment 50 grams of ortho-aminoacetophenone were dissolved in 100 grams of acetic anhydride. After standing in a freezing mixture for a few hours, the semi-crystalline mass was poured into 500 cc. of ice water. The acetyl derivative solidified at once. It was filtered off and washed numerous times with cold sodium

carbonate solution and then with water. Recrystallized from boiling water, it forms beautiful long white needles, m. p. 76°. 90% yield. The melting point corresponds to that given by Baeyer and Bloem.[6]

2,4-Dimethyl-quinazoline.—Fifty grams of the acetyl compound obtained above were heated with 250 grams of alcoholic ammonia in an autoclave for four hours at 150–160° as suggested by Bischler and Burkart.[11] After evaporating off the alcohol, the crude yellowish hydrate (27.5 gr., 50% yield) was dehydrated under diminished pressure, and the quinazoline then distilled. The first distillate was yellowish with a green fluorescence. On redistillation, the oil becomes colorless. When 2,4-dimethylquinazoline is pure, it has a very slight odor, when crude the odor is similar to crude acetamide. Because of its tendency to hydrate readily, it is necessary to keep it in a sealed bottle. B. p. 144° at 12 mm.; 143° at 11 mm.; 130–132° at 3 mm. Bischler and Burkart give its boiling point as 249° at 713 mm. Yield, 15 grams, 66%.

Attempts to Prepare Alkyl Iodide Addition Products of 2,4-Dimethyl-quinazoline.—To prepare these compounds, the following experiments were performed: 5.5 grams (1 mole) of 2,4-dimethyl-quinazoline together with 10 grams (2 moles) of methyl iodide and 19.8 grams of methyl alcohol were heated in a sealed tube for two hours at 120–130°C. The reaction mixture was a reddish liquid. This was poured from the tube, and the excess methyl iodide and alcohol allowed to evaporate spontaneously. The residue was brown and tarry. It was found to be impossible to isolate any crystalline product from this material.

Another experiment was tried in which the solvent was omitted and 1 mole each of methyl iodide and the quinazoline were heated in a sealed tube for seven hours at 110°. The reaction product was found to be a dark amorphous hard material. This could be recovered from the tube without the aid of a solvent. The product was ground to a fine powder. The excess methyl iodide was removed by boiling with amyl alcohol. The amorphous green powder which remained was extracted with acetone. The acetone became green in color,

and on standing deposited a light green fluffy substance. This was filtered off, washed with acetone, and immediately transferred to a vacuum desiccator. As soon as the acetone evaporated, there remained a dark green tar. Although the product was subjected to numerous solvents and mixtures of solvents to obtain a crystalline compound, all attempts were unsuccessful.

Other attempts to prepare an addition compound by varying the time of heating and the temperature, all proved unsatisfactory. An analysis was conducted on one of the reaction products, obtained by heating equal molecular amounts of methyl iodide and quinazoline in a sealed tube for three hours at 160°. The results, however, do not admit of any definite conclusions.

Analysis: Calc. for $C_{11}H_{13}N_2I$: C, 44.02; H, 4.36.
Found: C, 41.10, 41.87; H, 4.33, 4.97.

Since the direct addition of methyl iodide proved unsatisfactory, under the conditions of the experiments, dimethyl sulfate was used. In a typical experiment two grams of quinazoline were heated with 2.5 grams of dimethyl sulfate for four hours at 110–120°. A hard dark brown reaction product was obtained. This substance was dissolved in hot aqueous alcohol, and a saturated potassium iodide solution added. It was not possible to isolate any iodide addition product from the solution.

Attempts to Prepare Ethyl Iodide Addition Products of 2,4-Dimethyl-quinazoline.—Several attempts were made to prepare ethyl iodide addition products, but none of them proved fruitful. The conditions of experimentation and results were similar to those given above under the methyl iodide addition products.

Condensation Reactions with 2,4-Dimethyl-quinazoline.—Various attempts were made in an effort to condense benzaldehyde with 2,4-dimethyl-quinazoline, but these were not successful. In a typical experiment, two grams of the quinazoline were heated with 2.7 grams of freshly distilled benzaldehyde for ten hours at 150–160°. The mixture gradually changed from liquid to a dark viscous mass. Excess benzalde-

hyde was removed by steam distillation, and the dark brown tarry material remaining was dissolved out with glacial acetic acid. No crystalline substance could be obtained, although various solvents and mixtures of solvents were tried. Once a light yellow amorphous substance (0.2 gram) was isolated, m. p. 118–123°, recrystallized from alcohol. Analysis did not indicate any definite compound, and no more could be obtained, even though condensing agents were used as zinc chloride, acetic anhydride, the results could not be checked.

Analysis: Calc. for $C_{17}H_{14}N_2$: C, 82.9; H, 5.69.
Found: C, 80.89; H, 5.68.

2 grams of 2,4-dimethyl-quinazoline were allowed to react with 1.8 grams of *p*-dimethylaminobenzaldehyde in the presence of a few drops of piperidine. After boiling the alcoholic solution for ten hours, it was allowed to cool. No reaction product crystallized out, and so the alcohol was evaporated off. On purifying the residue it was found to consist of unreacted quinazoline in the form of its hydrate and *p*-dimethylaminobenzaldehyde in quantitative amounts.

2-Styryl-4-methyl-quinazoline.—This substance was prepared according to the directions given by Bischler and Howell.[12] 12 grams of *o*-cinnamylaminoacetophenone[8] were heated with alcoholic ammonia (five times the calculated amount) in a sealed tube for five hours at 150°. After evaporating off the alcohol, and recrystallizing from ethyl alcohol, 9.5 grams of silky needles were obtained, m. p. 96°. This is the same melting point as recorded by Bischler and Howell. Attempts to prepare methyl iodide addition products were not successful. When the sealed tube was opened it contained an orange sticky material which on standing became hard, m. p. 150–160°. It was not possible to purify this product.

2-Phenyl-4-methyl-quinazoline.—Pale yellow needles, m. p. 90°. Bischler and Howell record a melting point of 90°. Prepared according to the directions given by these authors.[13] (Furnished by the courtesy of Mr. F. B. Nabenhauer.)

Methyl iodide did not react with this substance. After heating equal molecular amounts of methyl iodide and quinazoline (1.8 gms.) in a sealed tube for two hours at 120°, 1.2

grams of material m. p. 90–91.5° were recovered. Mixed melting point showed this substance to be the original quinazoline. The experiment was repeated, this time heating for ten hours at 140–145°. A small amount of the original quinazoline was obtained.

B. Quinazolones

The following 4-quinazolone alkyl halides were prepared according to the directions given by Bogert and Geiger.[26,29]

3-Methyl-4-quinazolone Methyl Iodide.—This substance was prepared by heating 60 grams of 4-quinazolone[14] with 120 grams of methyl iodide in a sealed tube for 6.5 hours at 103°. The yellowish-red reaction product was recrystallized from methyl alcohol from which it separated in short, fine white needles. Yield 70 grams, or 56%, m. p. 271.4° (corr.). Bogert and Geiger give 269° (uncorr.) as the melting point.

2-Methyl-4-quinazolone Methyl Iodide.—Thirty-five grams of 2-methyl-4-quinazolone[19] were heated with 35 grams of methyl iodide in a sealed tube for seven hours at 150°. The yellow reaction product was dissolved out with the minimum amount of hot methyl alcohol. Recrystallized from a mixture of alcohol and ether cooled to —10°, short needles separated with slight yellow color, m. p. 223.7 (corr.). The melting point recorded by Bogert and Geiger is 220° (uncorr.). Yield, 23.5 grams, or 35%.

2,3-Dimethyl-4-quinazolone Methyl Iodide.[29]—To 20 grams of 2,3-dimethyl-4-quinazolone[19] were added 17 grams of methyl iodide, and the mixture heated in a sealed tube for 2.5 hours at 110°. The reaction product crystallized from methyl alcohol in short, white needles, m. p. 246° (corr.). The melting point given by Bogert and Geiger is 242° (uncorr.). Yield, 25 grams, or 80%.

2,3-Dimethyl-4-quinazolone Ethyl Iodide.[29]—The ethyl iodide addition product was prepared in a manner analogous to that of the methyl iodide given above. It melted at 241° (corr.). Bogert and Geiger give 237° (uncorr.). The yield was poor because of the extreme solubility of this compound in methyl alcohol.

2-Methyl-3-ethyl-4-quinazolone Methyl Iodide.[29]—In a typical preparation, 16 grams of 2-methyl-3-ethyl-4-quinazolone[19] were heated in a sealed tube with 13 grams of methyl iodide for four hours at 110°. On recrystallizing from methyl alcohol, the small yellowish needles were found to melt at 220° (corr.), while the melting point given by Bogert and Geiger is 217° (uncorr.). Yield, 11.5 grams or 41%.

Condensation Reactions for Preparation of Various 4-Quinazolone Isocyanine Iodides.—Ten grams of 2,3-dimethyl-4-quinazolone methyl iodide were heated with 8.65 grams of quinoline methyl iodide in 300 cc. methyl alcohol. When the solution began to boil, 1.3 grams of NaOH dissolved in a small amount of aqueous alcohol were added, and gentle boiling continued for one hour. The solution gradually assumed a deep red color. It was then placed in the dark, and allowed to cool slowly. After 96 hours, the crystalline needle-like precipitate (0.3 gram) was filtered off and washed several times with cold water, and then with cold alcohol. It was recrystallized from methyl alcohol, in which it is only slightly soluble. Small brown needles with a green metallic reflection crystallized out, m. p. above 365°, turning reddish at 310°. On examination under the microscope, the material was shown to be impure. An iodide determination did not allow of any definite conclusion being drawn as to the possible structure of the substance. This work was discontinued owing to the expense of the original material, and the unpromising results.

A similar experiment was carried out using 10 grams of ethyl iodide derivative of 2,3-dimethyl-4-quinazolone, 8.7 grams of quinoline ethyl iodide dissolved in 150 cc. absolute ethyl alcohol in which 0.75 gram of sodium ethylate (1.5 grams of sodium dissolved in 50 cc. absolute ethyl alcohol) was used as the condensing agent, but no crystalline material was obtained.

10 grams of 2,3-dimethyl-4-quinazolone methyl iodide were dissolved in 300 cc. methyl alcohol, together with 9.5 grams of quinaldine methyl iodide and 1.4 grams of NaOH (dissolved in a small amount of aqueous alcohol). The solution turned a deep purple. After boiling gently for 0.5 hour, it was placed in the dark to cool. The greenish-blue crystalline material

(0.4 gram) was removed by filtration after 96 hours, washed with water and methyl alcohol, and then melted at 290° with decomposition. Analysis showed this material to be identical with the 1,1′-dimethylcarbocyanine iodide + 1 mole CH_3OH, described by Pope and Mills.[33]

Analysis: Calc. for $C_{23}H_{21}N_2I + CH_3OH$: C, 59.51; H, 5.16.
Found: C, 59.72; H, 4.91.

In one case on evaporating the filtrate to a small volume, one gram of a greyish-white product was obtained. After several recrystallizations this material was shown to be unchanged 2,3-dimethyl-4-quinazolone methyl iodide.

All attempts to condense 2,3-dimethyl-4-quinazolone methyl iodide with itself were unsuccessful, although conditions were varied, and condensing agents such as pyridine,[38] sodium sulfide with chloroform,[45] sodium ethylate and sodium hydroxide with formaldehyde or chloroform,[42] were tried. In each instance, unchanged quinazolone was obtained.

***p*-Dimethylaminobenzaldehyde.**—This product was prepared according to the directions given by Adams and Coleman.[43] It crystallized from alcohol in yellowish-white plates, m. p. 73°.

(NOTE: Material used was prepared by Miss Katherine Lavers of Barnard College, and Mr. H. C. Nip of Columbia University.)

2-*p*-Dimethylaminostyryl-3-methyl-4-quinazolone Methyl Iodide.—Ten grams of 2,3-dimethyl-4-quinazolone methyl iodide, 4.7 grams of *p*-dimethylaminobenzaldehyde, and 1.5 grams of piperidine (freshly distilled) were dissolved in 300 cc. methyl alcohol and heated under a reflux for four hours. Allowed to cool slowly, a bright red crystalline precipitate (2.7 grams) separated and was filtered off after about 15 hours. It was washed several times with small amounts of ice cold methyl alcohol, and crystallized three times from methyl alcohol, in which it is very soluble. M. p. 216° (corr.) with evolution of gas.

Analysis: Calc. for $C_{20}H_{22}ON_3I$: C, 53.68; H, 4.96; I, 28.39.
Found: C, 53.76; H, 4.93; I, 28.52.

This red dye is soluble in methyl and ethyl alcohol, water, or acetone; slightly soluble in chloroform and benzene; insoluble in ether and ligroin. On allowing the filtrate to evaporate spontaneously, 2.9 grams of *p*-dimethylaminobenzaldehyde crystallized out, m. p. 73°. When the dye is dissolved in water, it gives an orange-red solution. The color disappears very quickly on the addition of a few drops of mineral acid. The solution turns pale yellow if a few drops of alkali are added. The decolorization of the aqueous dye solution by mineral acid is a characteristic of photosensitizing dyes. This substance, however, does not exhibit any marked photosensitizing properties (NOTE: Reported by the Eastman Kodak Co. Courtesy of Dr. C. E. K. Mees.) Silk or cotton immersed in a 1% dye bath, is dyed orange, and on washing with soap becomes pale yellow. The color is fugitive in the sunlight. Similar condensations were conducted replacing 2,3-dimethyl-4-quinazolone methyl iodide with 2-methyl-4-quinazolone methyl iodide; 2,3-dimethyl-4-quinazolone ethyl iodide, and 2-methyl-3-ethyl-4-quinazolone methyl iodide, and freshly distilled piperidine as a catalyst; but in each of these cases, the yield of condensation product was so small that it was decided to use acetic anhydride as the condensing agent. The products obtained from the piperidine condensations were all bright red needles.

2-*p*-Dimethylaminostyryl-4-quinazolone methyl iodide, m. p. 214°

2-*p*-Dimethylaminostyryl-3-methyl-4-quinazolone ethyl iodide, m. p. 205.5°

2-*p*-Dimethylaminostyryl-3-ethyl-4-quinazolone methyl iodide, m. p. 212°

Condensation Reactions of Various 4-Quinazolones in Acetic Anhydride

2-*p*-Dimethylaminostyryl-4-quinazolone Methyl Iodide.— Six grams (1 mole) of 2-methyl-4-quinazolone methyl iodide were dissolved in 50 cc. of acetic anhydride, together with 3 grams (1 mole) of *p*-dimethylaminobenzaldehyde. The solution was heated for two hours at 120–130°. On cooling,

reddish crystals (5.5 grams) separated. These were filtered off, washed several times with ice cold methyl alcohol and allowed to dry in the air. On recrystallizing from methyl alcohol (requires about 300 cc.), there were obtained 2 grams of reddish-purple needles. On examination under the microscope, these crystals appeared to be pure. Analysis, however, showed that the product was still impure. After washing carefully with 3 cc. amounts of warm methyl alcohol (in which it is only slightly soluble), and then drying for forty-eight hours in a KOH desiccator, it was found to be pure (1.9 grams). It begins to volatilize at 252°, decomposes at 255–265°, and melts at 265.7° (corr.) with evolution of gas.

Analysis: Calc. for $C_{19}H_{20}ON_3I$: C, 52.65; H, 4.64.
Found: C, 52.81; H, 4.71.

On evaporating the alcoholic filtrate, 3 grams of bright red needles were obtained. The product was recrystallized from methyl alcohol in which it is very soluble. Dried in a KOH desiccator for a few days, it melted at 214° (corr.). A mixed melting point, showed this substance to be identical with the product obtained in the piperidine condensation.

Analysis: Calc. for $C_{19}H_{20}ON_3I$: C, 52.65; H, 4.64.
Found: C, 52.34; H, 4.72.

It was found possible to regulate the acetic anhydride condensation reaction so that either one of the products obtained above could be obtained entirely free, or with only small amounts of the other.

To obtain the higher melting isomer, the acetic anhydride solution was heated for 2.0 to 2.5 hours at a temperature of 120° (±1°). If heating was continued for a longer time than this, a small amount of brown amorphous powder was formed, which melted at 250–260°. This material was not accumulated in sufficient amounts to permit of its identification.

The lower melting isomer was prepared by heating the acetic anhydride solution to 145° and keeping the temperature (145–150°) at this point for 0.25 hours. This isomer could be transformed into the higher melting substance by heating its acetic anhydride solution for a time at 120°. In a typical experi-

ment, one gram of material (m. p. 214°) was heated in 20 cc. acetic anhydride for two hours at 120–122°. There was obtained 0.8 gram of crude material which, after washing with methyl alcohol and drying, melted at 262–264°. This was recrystallized from methyl alcohol and dried in a KOH desiccator, when it melted at 265° with evolution of gas. A mixed melting point showed this substance and the higher melting isomer to be identical.

The higher melting isomer could not be changed into the lower melting form. It was exposed in a chloroform solution to 96 hours of summer sun, and finally 96 hours longer in a chloroform solution into which a crystal of iodine had been dropped. On evaporation of the chloroform and recrystallization from methyl alcohol, the material melted at 265°, and a mixed melting point showed it to be the unchanged higher melting isomer.

Although the two isomers are soluble in the same solvents, the lower melting isomer exhibits the greater solubility. They are soluble in methyl and ethyl alcohols, water, chloroform, acetone, acetic anhydride; slightly soluble in glacial acetic acid and benzene; insoluble in ether and ligroin. In dissolving the higher melting product in water, an orange solution results. If a few drops of mineral acid are added, the color slightly fades. Alkali turns the aqueous solution a lemon-yellow. The aqueous solution of the lower melting isomer, which is also orange, is decolorized immediately on the addition of a few drops of mineral acid, while alkali turns it a pale yellow.

Whether the condensation of the aldehyde could occur on the N—CH_3 group as well as on the C—CH_3 group was tested in the following manner. Three grams of 3-methyl-4-quinazolone methyl iodide and 1.5 grams of *p*-dimethylaminobenzaldehyde were heated in 25 cc. acetic anhydride for two hours at 120–130°. On cooling, a brownish crystalline mass separated. This was filtered and washed. On recrystallizing from methyl alcohol, there were obtained 2.7 grams of material, which was the original quinazolone, m. p. 263.4° (corr.). Evaporation of the filtrate yielded 1.3 grams of substance, m. p. 73°, which was *p*-dimethylaminobenzaldehyde. Hence, under

the conditions of experimentation, the aldehyde does not condense with the N—CH_3 group.

2-*p*-Dimethylaminostyryl-3-methyl-4-quinazolone Methyl Iodide.—Six and four-tenths grams of 2,3-dimethyl-4-quinazolone methyl iodide, and 3 grams of *p*-dimethylaminobenzaldehyde were heated in 200 cc. acetic anhydride for two hours at 125–130°. On cooling, there were obtained 4 grams of a purplish-red crystalline product. This was recrystallized from methyl alcohol. By evaporating down the filtrate from each crop of crystals, there were obtained three substances: (1) purplish-red needles m. p. 260–262.5° (with evolution of gas), 1 gram; (2) deep red powdery needles, m. p. 222.7–235°, 0.9 gram; (3) bright red needles m. p. 212–214°, 1.5 grams. When substance (1) was recrystallized from methyl alcohol and dried in a KOH desiccator, a substance resulted which started to volatilize at 250°, decomposed at 253–263°, and melted with evolution of gas at 263.5° (corr.).

Analysis: Calc. for $C_{20}H_{22}ON_3I$: C, 53.68; H, 4.96.
Found: C, 53.50; H, 5.12.

Substance (2) after several recrystallizations from methyl alcohol proved to be substance (1) with a small amount of brown amorphous material which was not identified.

When product (3) was recrystallized from methyl alcohol, bright red needles formed which melted at 216° (corr.). Mixed melting point and analysis, showed that this substance was identical with that obtained from the piperidine condensation.

Analysis: Calc. for $C_{20}H_{22}ON_3I$: C, 53.68; H, 4.96.
Found: C, 53.65, 53.62; H, 5.16, 5.19.

The bromine derivatives of the higher and lower melting isomers were shown to be identical by mixed melting points. (See below.)

It was possible to change the lower melting isomer into the higher melting product, by heating it for two hours at 120° with acetic anhydride. If the heating was continued for a longer time than this, a brown amorphous powder could be isolated.

Either one of these substances could be prepared without the other one by following the experimental details given above.

In the case of the lower melting product, it was necessary to continue the heating for twenty instead of fifteen minutes, or unchanged quinazolone was isolated in the crystalline product. The quinazolone could be washed out very readily with small amount of hot water in which it dissolves readily.

2-*p*-Dimethylaminostyryl-3-methyl-4-quinazolone Ethyl Iodide.—This substance was prepared in a manner similar to the methyl iodide product. 6.6 grams of 2,3-dimethyl-4-quinazolone ethyl iodide and 3 grams of *p*-dimethylaminobenzaldehyde, together with 50 cc. of acetic anhydride were heated for two hours at 120°. 5 grams of purple crystals were obtained. These were recrystallized from methyl alcohol. It was found to be extremely difficult to obtain a pure product; but, after washing numerous times with small amounts (3 cc.) of warm methyl alcohol, and drying in a KOH desiccator, a product which analyzed consistently was formed. Purplish-red needles (2 grams), which volatilized at 255°, decomposed at 257–264°, and melted at 264.7° (corr.) with evolution of gas.

Analysis: Calc. for $C_{21}H_{24}ON_3I$: C, 54.65; H, 5.21.
Found: C, 54.68; H, 5.11.

To prepare the lower melting isomer, 6.6 grams of 2,3-dimethyl-4-quinazolone ethyl iodide and 3 grams of *p*-dimethylaminobenzaldehyde, together with 50 cc. of acetic anhydride, were heated for ten minutes at 145–150°. The reaction became quite vigorous and lasted for five minutes. On cooling, a bright red pasty mass separated. After filtering, drying, and recrystallizing from methyl alcohol, the product was found to be identical (mixed melting point) with the bright red needles obtained from the piperidine condensation. M. p. 205.5°. Yield, 5 grams.

Analysis: Calc. for $C_{21}H_{24}ON_3I$: C, 54.65; H, 5.21.
Found: C, 54.71; H, 5.19.

As in the case of the other substances, the lower melting isomer could be transformed into the higher melting product by prolonged heating (2 hours) with acetic anhydride at 120°.

2-*p*-Dimethylaminostyryl-3-ethyl-4-quinazolone Methyl Iodide.—The lower and higher melting isomers of this substance were made to determine whether interchanging the position

of the alkyl groups had an effect on photosensitizing properties.

Six and six-tenth grams of 2-methyl-3-ethyl-4-quinazolone methyl iodide, and 3 grams of *p*-dimethylaminobenzaldehyde were heated in 50 cc. acetic anhydride for ten minutes at 145–150°. On cooling, bright red needles formed, which when dry had a bluish reflection. The product was recrystallized from methyl alcohol and dried over KOH, m. p. 212°. Yield, 4 grams. Mixed melting point showed this substance to be identical with the one obtained from the piperidine condensation.

Analysis: Calc. for $C_{21}H_{24}ON_3I$; C, 54.65; H, 5.21.
Found: C, 54.91; H, 5.50.

Two grams of the material prepared above were heated in 25 cc. of acetic anhydride for two hours at 120°. When cold, purplish-red crystals formed (0.9 gram). This product was recrystallized from methyl alcohol, and dried over KOH. It volatilizes at 245°, decomposes at 247–254°, and melts with evolution of gas at 255° (corr.).

Analysis: Calc. for $C_{21}H_{24}ON_3I$: C, 54.65; H, 5.21; I, 27.54.
Found: C, 54.26; H, 5.29; I, 27.52.

The higher melting isomer dyes both silk and cotton. After soaking the materials in a 1% dye bath for thirty minutes, they were dyed a pale orange. On rinsing and washing in soapy water, they turned a pale canary-yellow. The color is fugitive in the sunlight, but after remaining in the dark for two weeks, it gradually returned. The lower melting isomer dyes a paler shade, and the color faded by the sunlight does not seem to return.

Bromine Derivatives.—Two and three-tenths grams of the lower melting isomer of the above substance were dissolved in 100 cc. of chloroform, and the solution cooled to 5° C. To this was added drop by drop a cold solution of bromine (0.7 gram) in chloroform. The deep red solution gradually loses its color, and hydrogen bromide is evolved. When all of the bromine had been added the solution was cloudy orange. This was poured onto a watch glass and the chloroform evaporated off with a rapid stream of air. The orange amorphous powder (2.5 grams) was dissolved in methyl alcohol, from which minute

needles separated (2 grams), melting at 146–150° with evolution of gas. An examination under the microscope showed the crystalline material to consist of short thick red needles and long fine yellowish-orange ones. These could be separated by their different solubilities in methyl alcohol, the red needles being the most soluble. After six recrystallizations from methyl alcohol, the red needles were shown to be unchanged dye (m. p. 212° corr.) and yellowish-orange needles (0.4 gram) m. p. 152° (corr.).

Analysis: Calc. for $C_{21}H_{23}ON_3Br_3I$: C, 36.02; H, 3.32; Br, 34.26.
Found: C, 36.55, 36.48; H, 3.71, 3.75; Br, 34.51.

A similar experiment was performed with the higher melting isomer using 0.4 gram, dissolved in 50 cc. of chloroform and adding the calculated amount of bromine in chloroform solution. An orange crystalline product remained after evaporation of the chloroform. This was recrystallized twice from methyl alcohol, and then melted at 152° (corr.). This substance is identical with the tribromo derivative from the lower melting isomer, as determined by a mixed melting point.

The tribromo derivative of the higher and lower melting isomers of 2-*p*-dimethylaminostyryl-3-methyl-4-quinazolone methyl iodide were prepared in a similar manner. These substances form orange needles melting at 178° (corr.).

Analysis: Calc. for $C_{20}H_{21}ON_3Br_3I$: C, 35.06; H, 3.09.
Found: C, 34.95; H, 3.15.

The bromine derivatives of 2-*p*-dimethylaminostyryl-4-quinazolone methyl iodide and 2-*p*-dimethylaminostyryl-3-methyl-4-quinazolone ethyl iodide were not prepared, except in a qualitative way, because of insufficient material of both pairs of isomers.

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BIOGRAPHICAL

Helen Clark was born in Brooklyn, N. Y., November 19, 1896. She entered Adelphi College in 1915. After one year at this institution, she became a pupil dietitian at Greenpoint Hospital. The following year, 1917–18, she was an assistant chemist for the General Chemical Company. In 1918, she transferred to Teacher's College, from which she received the degree of B.S. in 1920. Since that time she has furthered her graduate studies under the Faculty of Pure Science of Columbia University, from which she received the degree of M. A. in 1921. During this period she has held the assistantship in chemistry at Barnard College.